Researching Brown Adipose Tissue to Treat Diabetes

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While obesity and Type 2 Diabetes were once considered diseases of the wealthy, they now affect other populations. The availability of processed foods has led to a vicious cycle of weight gain and disease among the poor, children, and across developing countries, resulting in a complex public health crisis that requires action on several fronts. Exercise, modified diets, and medications are all part of the armamentarium of modern endocrinologists and nutritionists who fight this ongoing battle.

The key therapeutic goal is as simple in concept as it is difficult to achieve—improve a patient’s energy balance so that more calories are burned than consumed. For the past four decades, one goal has been to increase energy expenditure by activating a patient’s brown adipose tissue (BAT), also known as brown fat. In smaller animals, BAT has two related roles: to protect against cold exposure and maintain energy balance by consuming glucose and fat to generate heat. Though small in size, maximally activated BAT can account for 20 percent of a mouse’s metabolic rate. It was once believed that adult humans do not have BAT.

This dogma was overturned four years ago, when multidisciplinary teams discovered that PET/CT imaging used for cancer surveillance was broadcasting the presence of active BAT in adult humans. Leading one of the teams to report these findings in the New England Journal of Medicine was Aaron M. Cypess, MD, PhD, MMSc, who holds dual appointments in the Division of Endocrinology at Beth Israel Deaconess Medical Center (BIDMC) and the Research Division of Joslin Diabetes Center. The next challenge: translate this discovery into treatments for patients with obesity and metabolic disease.

Working in conjunction with research dietitians, nurses, and lab personnel at the Harvard Catalyst Clinical Research Center at BIDMC, Cypess recently showed that patients with mild cold exposure (wearing a cooling vest) could expend as many calories as they did while on the weight loss drug ephedrine, but with minimal side effects. Encouraged by these results, Cypess assembled a multidisciplinary team and expanded his research platform to evaluate the effectiveness of novel drugs and hormones that activate BAT. These studies were developed with the guidance of Harvard Catalyst biostatistical and IND consulting, and some of the projects have had direct support from the pilot and feasibility program. As he prepares to conduct large clinical trials to evaluate the effects of long-term stimulation of BAT, Cypess is optimistic about the possibilities of using BAT’s calorie-burning potential for patients to lose weight and treat diabetes.
Scheduler: Now Live at MGH & BWH

The HCCRC Scheduler system launched at Massachusetts General Hospital (MGH) in November and at Brigham and Women’s Hospital (BWH) in December. The system, which has been operating at BIDMC since 2012, allows study staff to schedule research subjects independently without having to directly contact CRC scheduling staff. The team for the MGH roll-out included Sarah Luthern, Liz Graber, Ellen Anderson, Edwin Andrews, and Kathy Hall. The BWH roll-out team included Yemi Talabi-Oates, Joanna Waterfall, Michelle Song, Joyce Clark, Sheila Driscoll, Leigh Keating, and Kris Jordan. Both teams partnered with Bridget Gaffney, Richie Siburian, Thomas Naughton, and Joanna Brownstein from the HCCRC Informatics Team. The system has been working for several weeks and the initial response has been quite positive.

The Scheduler was developed as a collaboration between the Harvard Catalyst Clinical Research Center Program, Harvard Catalyst Informatics, and representatives from the CRCs at Boston Children’s Hospital (BCH), BIDMC, BWH and MGH. BCH is slated to go live in early 2014.

New: Guidance for Investigators on Using the HCCRC

When investigators meet with the HCCRC staff to operationalize new studies, they will receive the new Guidance for Investigators. The document contains helpful guidelines and general information to ensure that every research participant and investigator has a positive and safe experience, and guidance on priming the protocol for success. Also included are guidelines around communication, study implementation, safety, and citation language. Additional docs include the protocol change request form, and documents to facilitate discussion on budgets, and a service request summary.

Policy Change for Laboratory Assay Support

HCCRC support for laboratory testing continues to be available to investigators whose studies have been approved through the Protocol Review system to use the HCCRC resources for inpatient, outpatient, or off-unit research visits. The Harvard Catalyst grant is able to support laboratory testing costs based on the annual availability of funds.

All protocols submitted to the HCCRC Protocol Review system after December 1, 2013 that request HCCRC support for laboratory assays will be subject to the following new support guidelines:

- Junior investigator-initiated studies will be eligible for up to $50 in per-visit assay support
- Senior investigator-initiated studies will be eligible for up to $20 in per-visit assay support

There will be no change to the current types of assays supported, regardless of their use as endpoints or for safety/screening/dosage. Studies which have been submitted to protocol review on or prior to November 30, 2013 will continue to be supported at current levels (junior investigators: $60/visit; senior investigators: $30/visit) until April 30, 2014. All protocols will be required to adjust to the revised policy as of May 1, 2014.

Please speak with your HCCRC site administrative director regarding how this policy change may affect your HCCRC protocol.

Medical Research Officers Facilitate Cross-institutional CRC Use

While Medical Research Officers (MROs) support institution-credentialed investigators studies, providing them with coverage for travel and other needs, they also assist investigators who are not medically credentialed at that institution. For investigators not credentialed at a given institution, the MRO can help facilitate minimal risk blood draws and routine questionnaires. Although they don't function as members of the research team, their role is to act similar to core service providers. When making a request, the MROs will assess each individually to determine whether it meets the risk criteria established by the IRBs.

Each HCCRC site has an MRO available to assist investigators with both clinical support as well as general clinical research consultations. Contact Evan Gwyn for BIDMC, Stavroula Osganian for BCH, Madhu Misra for MGH, and Gail Adler for BWH.
The Mentored Clinical Research Experience

For scientists who work in basic research, moving to the clinical side can be a daunting endeavor. To address these barriers, a pilot course was offered last fall to give basic science researchers an opportunity to learn the process of setting up a clinical and translational research study at the Harvard Catalyst Clinical Research Centers (CRC). The CRCs are located at four area hospitals: Beth Israel Deaconess Medical Center (BIDMC), Brigham and Women’s Hospital (BWH), Massachusetts General Hospital (MGH), and Boston Children’s Hospital (BCH). Co-sponsored by the Harvard Catalyst Education and Training program, the Mentored Clinical Research Experience (MCRE) provided a hands-on, interactive twelve-week program to four non-clinical PhDs interested in exploring the transition to clinical research.

During the course, participants were matched with clinical research mentors, made regular visits to the CRCs, and met as a group to discuss their experiences and learn about various topics pertinent to clinical research. To keep the focus on process rather than scientific area of interest, each student was matched with a mentor who had a different research background. Participants also made a series of visits to the CRC of the mentor’s institution to take a comprehensive tour, meet key personnel, review the consent process, interact with CRC study subjects, and learn how to access resources and fund their studies.

Frequent group meetings facilitated by the MCRE curriculum committee members created an atmosphere of collaborative learning. Participants also took part in presentations and dialogues with guest speakers including Sabune Winkler, JD; Julie Buring, D.Sci; and Josh Roffman, MD, who presented on topics including the IRB process, ethical considerations in clinical research, study design best practices, and regulatory compliance.

For more information, please visit the course website.

CRC updates

The majority of our services are free up to a specific level, beyond which there may be a fee based on time and complexity.

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HCCRC @ MGH

In the News

Recently an article on the front page of the New York Times featured a study on the effect of estrogen on middle-aged men. Joel Finklestein, MD, conducted long-term studies at the MGH. He and his team used MGH CRC resources, including assistance of expert CRC metabolism and nutrition research (MNR) and nursing staff to implement the study protocol. These studies are the start of what many hope will be a new understanding of the roles of testosterone and estrogen in men. They are typical of the type of endocrine studies that have driven CRC activity at the MGH for many years and have helped provide insight into normal human function, as well as into disease states.

Connell Scholars

The highly competitive Connell Nursing Research Scholars Program selected four nurse practitioners to take part in their year-long program, two of which are staff members at MGH CRC. The program allows each participant dedicated time each week to advance a research agenda consistent with the strategic goals of MGH Patient Care Services and their personal research focus.

Mary Sullivan PhD, ANP, BC, is investigating catheter-associated urinary tract infections in the ICU and develop a nursing intervention aimed at decreasing these rates within MGH’s ICUs. Katherine Rosa, PhD, FNP-BC, plans to examine the effectiveness of a relationship-based nursing intervention on facilitating lifestyle behavior changes in persons living with chronic illnesses.

Stephanie Ball, RN, and Sara Looby, PhD, who has conducted research on the MGH CRC, are the other two recipients.

Fifth International Association of Clinical Research Nurses (IACRN) Conference

In late October, MGH nurses, including those from the MGH CRC, attended and presented their work at the fifth annual International Association of Clinical Research Nurses (IACRN) Conference in San Diego, California.

Catherine Griffith, PhD(c), ACNP-BC, presented a project and also a poster with Sharon Maginnis, BS. This poster was co-authored by Audrey Nathanson, RN, Tracy Cragin, RN, Sheila Driscoll, Mona Lauture, RN, and Ivy Dang, RN.

Kathryn Hall, MS, ANP-BC, nurse director of the MGH CRC presented a poster and also gave a talk with her fellow Harvard Catalyst nurse directors Sheila Driscoll MS, RN, nurse director at the BWH CRC and Linda Godfrey Bailey, MSN, ACNS, BC, nurse director at the BIDMC CRC.

HCCRC @ BWH

The Brigham Research Assay Core (BRAC) Offers CDC-Certified LC-MS/MS Assays

The Brigham Research Assay Core (BRAC) officially opened its doors as an assay laboratory this past November with the merger of three entities—the former Harvard Catalyst Core Laboratory (HCCL), LCMS/MS Laboratory, and Specialty Assay Research Core (SARC). The mission of the BRAC Laboratory is to provide a comprehensive menu of state-of-the-art research assays to the Partners and non-Partners research communities at competitive costs. The BRAC Laboratory is a dynamic entity seeking to meet the needs of its investigators by offering new and relevant technologies and evolving research support.

Currently BRAC employs five technological platforms: immunoassays, liquid chromatography tandem mass spectrometry (LC-MS/MS) and other MS-based technologies, free hormone measurements using equilibrium dialysis, and blood chemistries.

The following assays are now available using the LC-MS/MS platform: Testosterone, 25-hydroxyvitamin D2 and D3, Estradiol, Estrone, para-amino-hippuric acid (PAH) and dihydrotestosterone (DHT). Several additional LC-MS/MS assays are currently under development.

In addition to human samples, BRAC also can perform assays on non-human specimens. BRAC is a CLIA-certified laboratory and is accredited by the Joint Commission. The BRAC sex-steroid assays are certified by the Centers for Disease Control’s Steroid Hormone Assay harmonization Program. BRAC is one of only a handful of academic laboratories to receive CDC certification, which requires a substantially higher level of accuracy and stringency than CLIA certification.

In addition to its current menu of assays, BRAC offers individualized consulting, and custom design and development of new LC-MS/MS assays. Please contact Shalender Bhasin, MD, director or Bharti Thakkar, MBA C(ASCP), laboratory manager with questions. Further information is available at the BRAC website.